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(71) Applicant *(for all designated States except US)*: UNIVERSITY OF CONNECTICUT [US/US]; 263 Farmington Avenue, Farmington, CT 06032 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: MAKRIYANNIS, Alexandros [US/US]; 348G Foster Drive, Willimantic, CT 06226 (US). LIU, Qian [CN/US]; 1 Northwood Road, Apt. 25, Storrs, CT 06268 (US).

(74) Agents: YALE, Guy, D. et al.; Alix, Yale & Ristas, LLP, 750 Main Street, Hartford, CT 06103 (US).

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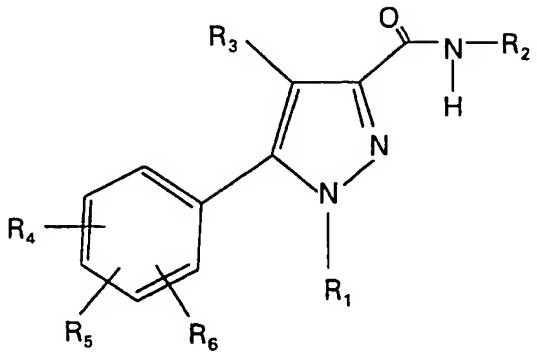
(54) Title: PYRAZOLE DERIVATIVES AS CANNABINOID RECEPTOR ANTAGONISTS

(57) Abstract: Novel cannabimimetic pyrazole derivatives are presented which have preferentially high affinities for both of the cannabinoid CB1 or CB2 receptor sites. The improved receptor affinity makes these analogs useful as experimental tools for cannabinoid receptor studies as well as clinically useful agents in individuals and animals for treatment of memory deficits associated with aging or neurological diseases, as anti-obesity agents, as medications for schizophrenia and treatment of septic shock syndrome.

What Is Claimed Is:

1. A compound of the formula



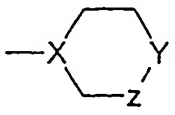
or a physiologically acceptable salt thereof, wherein:

R_1 is a branched or unbranched chain having the structure $(CH_2)_nZ$ where n is an integer from 1 to about 10 and Z is selected from the group consisting of H, halogen, N_3, NCS, CN, OH, OCH_3, NH_2 and $CH=CH_2$;

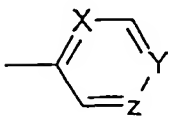
R_3 is selected from the group consisting of H and a branched or unbranched chain having the structure $(CH_2)_nCH_3$ where n is an integer from 0 to about 3;

R_4, R_5 and R_6 are each selected from the group consisting of halogen, N_3, NCS, OCH_3, CH_3, CH_2CH_3, NO_2, NH_2, phenyl and phenyl with at least one substituent from the group consisting of halogen, N_3, NCS, OCH_3, CH_3, CH_2CH_3, NO_2, and NH_2; and

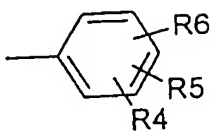
R_2 is selected from the group consisting of napthyl,



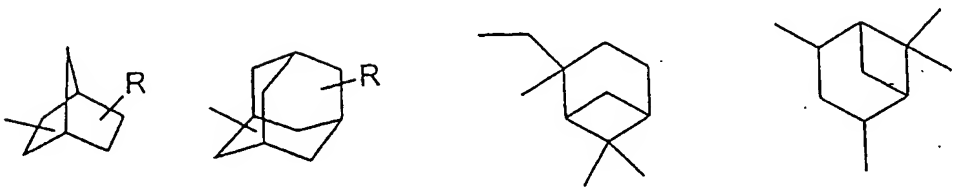
where X is selected from the group consisting of N and CH and Y and Z are each selected from the group consisting of O, N, S and $(CH_2)_n$ where n is an integer from 1 to about 7,



where X, Y and Z are each selected from the group consisting of N and CH,

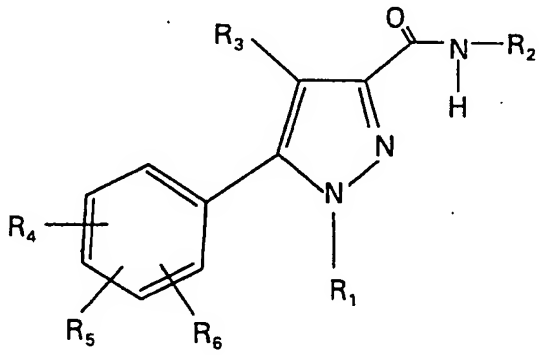


where R_4, R_5 and R_6 are each selected from the group consisting of halogen, N_3, NCS, OCH_3, CH_3, CH_2CH_3, NO_2, NH_2 and phenyl,



where R is selected from the group consisting of H, halogen, N_3, NCS, CN, OH, OCH_3, NH_2 and $CH=CH_2$.

2. A method of preferentially binding to the cannabinoid receptors in an individual or animal comprising administering to the individual or animal a therapeutically effective amount of a compound having the formula

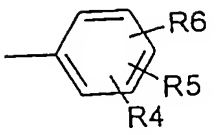


and physiologically acceptable salts thereof, wherein:

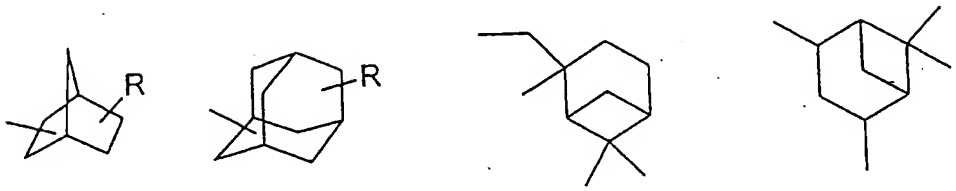
R_1 is a branched or unbranched chain having the structure $(CH_2)_nZ$ where n is an integer from 1 to about 10 and Z is selected from the group consisting of H, halogen, N_3, NCS, CN, OH, OCH_3, NH_2 and $CH=CH_2$;

R_3 is selected from the group consisting of H and a branched or unbranched chain having the structure $(CH_2)_nCH_3$ where n is an integer from 0 to about 3;

R_4, R_5 and R_6 are each selected from the group consisting of halogen,

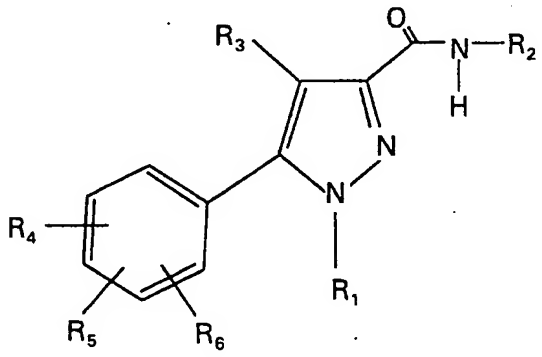


where R_4, R_5 and R_6 are each selected from the group consisting of halogen, N_3, NCS, OCH_3, CH_3, CH_2CH_3, NO_2, NH_2 and phenyl,



where R is selected from the group consisting of H, halogen, N_3, NCS, CN, OH, OCH_3, NH_2 and $CH=CH_2$.

2. A method of preferentially binding to the cannabinoid receptors in an individual or animal comprising administering to the individual or animal a therapeutically effective amount of a compound having the formula



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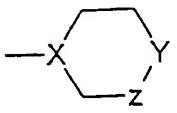
R_1 is a branched or unbranched chain having the structure $(CH_2)_nZ$ where n is an integer from 1 to about 10 and Z is selected from the group consisting of H, halogen, N_3, NCS, CN, OH, OCH_3, NH_2 and $CH=CH_2$;

R_3 is selected from the group consisting of H and a branched or unbranched chain having the structure $(CH_2)_nCH_3$ where n is an integer from 0 to about 3;

R_4, R_5 and R_6 are each selected from the group consisting of halogen,

N_3, NCS, OCH_3, CH_3, CH_2CH_3, NO_2, NH_2, phenyl and phenyl with at least one substituent from the group consisting of halogen, N_3, NCS, OCH_3, CH_3, CH_2CH_3, NO_2, and NH_2; and

R_2 is selected from the group consisting of napthyl,



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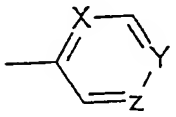
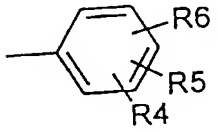
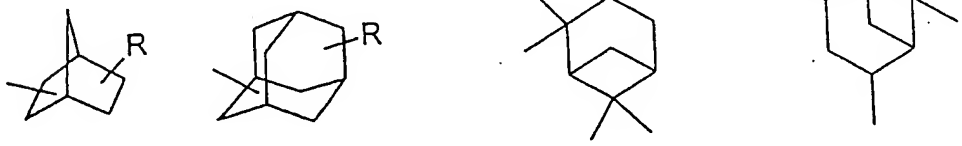


where X, Y and Z are each selected from the group consisting of N and CH,

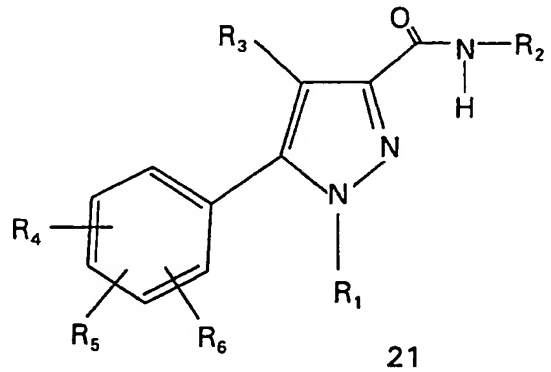


where R_4, R_5 and R_6 are each selected from the group consisting of halogen, N_3, NCS, OCH_3, CH_3, CH_2CH_3, NO_2, NH_2, phenyl and



where R is selected from the group consisting of H, halogen, N_3, NCS, CN, OH, OCH_3, NH_2 and $CH=CH_2$.

3. A pharmaceutical composition containing a therapeutically effective amount of a compound having the formula



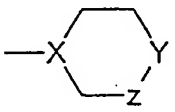
and physiologically acceptable salts thereof, wherein:

R_1 is a branched or unbranched chain having the structure $(CH_2)_nZ$ where n is an integer from 1 to about 10 and Z is selected from the group consisting of H, halogen, N_3, NCS, CN, OH, OCH_3, NH_2 and $CH=CH_2$;

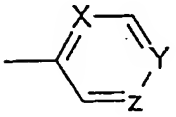
R_3 is selected from the group consisting of H and a branched or unbranched chain having the structure $(CH_2)_nCH_3$ where n is an integer from 0 to about 3;

R_4, R_5 and R_6 are each selected from the group consisting of halogen, N_3, NCS, OCH_3, CH_3, CH_2CH_3, NO_2, NH_2, phenyl and phenyl with at least one substituent from the group consisting of halogen, N_3, NCS, OCH_3, CH_3, CH_2CH_3, NO_2, and NH_2; and

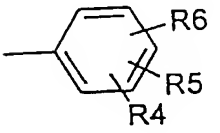
R_2 is selected from the group consisting of napthyl,



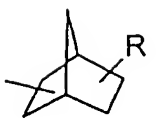
where X is selected from the group consisting of N and Ch and Y and Z are each selected from the group consisting of O, N, S and $(CH_2)_n$ where n is an integer from 1to about 7,

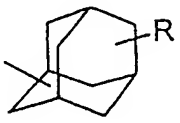


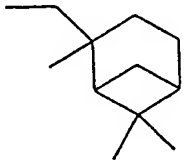
where X, Y and Z are each selected from the group consisting of N and CH,

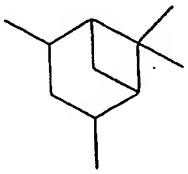


where R_4, R_5 and R_6 are each selected from the group consisting of halogen, N_3, NCS, OCH_3, CH_3, CH_2CH_3, NO_2, NH_2, phenyl and









where R is selected from the group consisting of H, halogen, N_3, NCS, CN, OH, OCH_3, NH_2 and $CH=CH_2$.